

Global Perspective on Kidney Transplantation: Brazil

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Introduction

Brazil is a country with 211 million inhabitants distributed within an area of 8,200,000 km². There are 27 states distributed in five administrative regions: North, North-East, Central-West, South-East, and South. In 2020, the annual gross domestic product (GDP) was 2.0 trillion US dollars, yielding an average of 11,000 US dollars per capita, ranking the Brazilian economy as the 12th largest in the world (1).

Financing of the Health System in Brazil

The Brazilian health care system comprises a large public, government-managed system (Sistema Único de Saúde), which serves the majority of the population. Expenditure on health care is approximately 9% of the GDP (1), derived from federal, state, and municipal taxation and from Ministry of Health subsidies. The private health care sector covers about 28% of the population. Brazil has developed successful models of government funded, high complexity, and high-cost health care assistance programs beyond the expectations of a developing country. Among them is the National Transplant System (NTS), which accounts for over 95% of the transplant surgery reimbursements and provides immunosuppressive drug coverage for all patients (2).

There are few analyses in terms of economy, but one publication suggests that there is an advantage in terms of cost when kidney transplantation is compared to other modalities of renal replacement therapy (3).

Patients on Dialysis and on the Transplant Waiting List

In July 2018, according to the Brazilian Census of Dialysis, the estimated total number of patients on dialysis was 133,464, with an estimated prevalence rate of 640 patients per million population (pmp). Of the prevalent patients, 92.3% were on hemodialysis and 7.7% were on peritoneal dialysis, with 29,545 (22.1%) of them on the transplant waiting list (4). The median waiting time for a deceased donor kidney transplant is 3 years.

The National Transplant System

The first kidney transplant was performed in 1964, followed by heart, liver, and pancreas transplants in

1968, and lung transplants in 1989. The first law regulating organ procurement and transplantation was instituted in 1963, and the current legislation dates from 1997. This legislation instituted the National Transplant System, a federal organism subordinated to the Ministry of Health that regulates and coordinates all organ donation and transplantation activities in a decentralized fashion at the state level.

The current legislation allows living donor transplantation from relatives up to fourth-degree and spouses with least 21 years of age. There is no specific determination of the minimum duration of the marriage. In order to avoid marriage only for transplantation, all cases of transplantation between spouses are analyzed by the Public Prosecutor's Office. Unrelated donors need judicial authorization. Only ABO blood group system compatible transplants with a negative crossmatch are performed. Altruistic donor chains and paired donations are forbidden by the existing legislation.

Deceased organ donors are procured by the Notification, Donation and Procurement Central Office (CNCDO), located at each State Health Secretary. Each of the Notification, Donation and Procurement Central Offices coordinates the activities of one or more organ procurement organizations, public agencies, and in-hospital coordinators, depending on regional aspects and population density. The legal framework for brain death is based on international clinical criteria supported by complementary laboratory tests. Informed family consent is required for all deceased donors. Currently, donations after circulatory death and the use of HIV-positive deceased donors are not legally supported. Once authorized by the family, organ recovery is orchestrated by the organ procurement organizations, with urologists usually performing organ recovery.

The allocation system is based on a single regional waiting list for each organ. Kidneys are allocated based on ABO blood group system identity and human leukocyte antigen matching, and organs from donors younger than 18 years are primarily allocated to pediatric recipients. Patients with precarious vascular access for hemodialysis and medical contraindications for or failure of peritoneal dialysis have priority for kidney transplantation. In some states of the country, family members of donors also have

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	Central-West	North-East	North	South-East	South
Population (2020), n	16,297,074	57,071,654	18,430,980	88,371,433	29,975,984
GDP per capita (2020), US dollars	11,119	4,495	5,430	11,294	10,320
Patients in dialysis (2018), n	10,560	30,247	8,257	65,218	18,645
Patients in the waiting list (2020), n	312	3,194	431	19,932	2,565
Effective donors (2020), pmp	11.2	9.0	2.1	18.6	31.4
Familiar refusal (2020), %	54%	51%	53%	42%	30%
Kidney transplants (2020) pmp	18.7	12.5	0.9	30.9	34.7

Figure 1. | Major socioeconomic and health-related indicators, showing the regional inequalities in Brazil, with the southern and south-eastern regions showing better socioeconomic performance and with respect to transplantation.

priority. The organs from deceased donors are allocated at the regional level. In the absence of a compatible recipient and fit for transplantation, these organs are then distributed at the national level. Urologists, general surgeons or vascular surgeons perform organ recovery and the kidney transplant surgery. Generally, the patient is followed by the surgical team plus nephrologists during the hospitalization after surgery and, after the discharge, is followed by a dedicated team of nephrologists.

The allocation of the organs at the state level partially limits the displacement of the organ. In addition, the patient travels to the transplant center, which also minimizes cold ischemia time. Nevertheless, the average national cold ischemia time is long, about 22 hours.

Transplant Numbers and Outcomes

Created in 1986, the Brazilian Association of Organ Transplantation is a nonprofit civil medical society whose mission is to stimulate the development of all activities related to organ transplantation, contributing to the establishment of standards and guidelines, in addition to creating and improving legislation related to the subject. The society also coordinates the national transplant registry report, including state level data from donors and all organ transplants.

The absolute volume of the national transplant program is surpassed only by the United States. Over the past

8 years, the notification rate of potential donors has increased 28% and the effective donor rate has grown 49%, going from 13.2 donors per million population (pmp) in 2013 to 18.1 donors pmp in 2019. The family refusal rate has remained at 42% in the last 5 years and is mainly due to the still incomplete understanding of the diagnosis of brain death within the society. In 2019, there were 6283 kidney transplants (30 pmp) performed, 50% of the estimated 12,510 transplants needed (60 pmp). Between 54% and 71% of recipients of deceased donor kidney transplants develop delayed graft function. This high incidence is a consequence of relatively late donor referral, inadequate donor maintenance and long cold ischemia times (5).

There are significant disparities in access to dialysis, waiting lists, and kidney transplantation within the national regions, with the North, North-East and Central-West regions showing inferior performance (Figure 1). Although the South region has 31.4 effective donors pmp, a figure comparable to Spain, the North regions have only 2.1 effective donors pmp (6). Such discrepancies may be related to the historical concentration of income, as reflected by the GDP per capita and technology in the South and Southeast regions of the country, all impacting the structure and the organization of the health care system, access to dialysis services and the waiting list, as well as the number and preparedness of trained teams for organ recovery, transplantation, and follow-up.

In 2020, the coronavirus pandemic produced a significant negative impact on national transplant activity. There were 4805 kidney transplants performed, an overall reduction of 24.5% compared with the previous year. This decrease was smaller in the Central-West (20%) and South-East (32%) regions but was more pronounced in the South (39%) and North-East (45%) regions and profound in the North (66%). In most centers, the living donor kidney transplant program was severely restricted or interrupted. The number of living donor kidney transplants performed in 2020 ($n=440$) reached its lowest since 1984, when 495 living donor kidney transplants were performed.

Immunosuppression protocols in Brazil generally include induction with an anti-IL2 antibody (basiliximab) or an antibody antilymphocyte (r-ATG). Most transplant centers use calcineurin inhibitors, and tacrolimus is the most frequently prescribed medication. Also, most centers use steroids, with maintenance doses around 5 mg/day of prednisone or equivalent. Mycophenolate, azathioprine, sirolimus or everolimus are used as the third immunosuppressive drug, and the choice for one drug or another depends on the perception in relation to the characteristics of the donor, the degree of sensitization of the recipient, and the risk of cytomegalovirus disease, among other factors.

Several single-center analyses suggest progressive and continuous improvement in patient and graft survival over the years, one key measure of the consolidation of the national program. Based on data from 71 out of 127 active transplant centers in 2020, the Brazilian Registry of Transplantation reported 1-, 5-, and 10-year graft survival rates of 94%, 86%, and 76% for living donor and 88%, 76%, and 64% for deceased donor kidney transplants, respectively (6).

Areas of Improvement

Although Brazil has a well-consolidated national organ transplant program with large volume and improving survival outcomes, strategies to reduce the regional disparities is paramount.

From access to dialysis and to the waiting list, investments in the health care system are needed in the North, North-East, and Central-West regions, since the main barrier to access to kidney transplantation is not a negative attitude to the expected quality of life after transplantation but the lack or low activity of organ extraction and transplant teams in these regions. Policies are needed to ensure the access of patients with ESKD to dialysis services and referral for kidney transplant centers. This investment should be directed to increase local infrastructure, increase the number and capacitation of the professionals, and to promote educational activities to the society. This strategy should focus on the early identification of potential donors, diagnosis of brain death, and donor maintenance. Campaigns to increase awareness of the concept of brain death and the beneficial effect of organ donation should be disseminated to society.

Further improvements in allocation algorithms of organs recovered from expanded criteria donors and priority criteria for hypersensitized patients, beyond human leukocyte

antigen matching, have been discussed. Finally, measures to reduce the burden of several endemic diseases and non-adherence to immunosuppressive medications are essential to improve long-term transplant outcomes.

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Author Contributions

M. Cristelli and J. Medina-Pestana conceptualized the study; M. Cristelli was responsible for data curation; M. Cristelli and G. Ferreira were responsible for formal analysis; M. Cristelli, G. Ferreira, and J. Medina-Pestana wrote the original draft; G. Ferreira was responsible for visualization; and M. Cristelli, G. Ferreira, and J. Medina-Pestana reviewed and edited the manuscript.

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